

*Invited Editorial*

**Potential Strategies to Improve Antimicrobial Utilisation in Hospitals in Bangladesh Building on Experiences Across Developing Countries**

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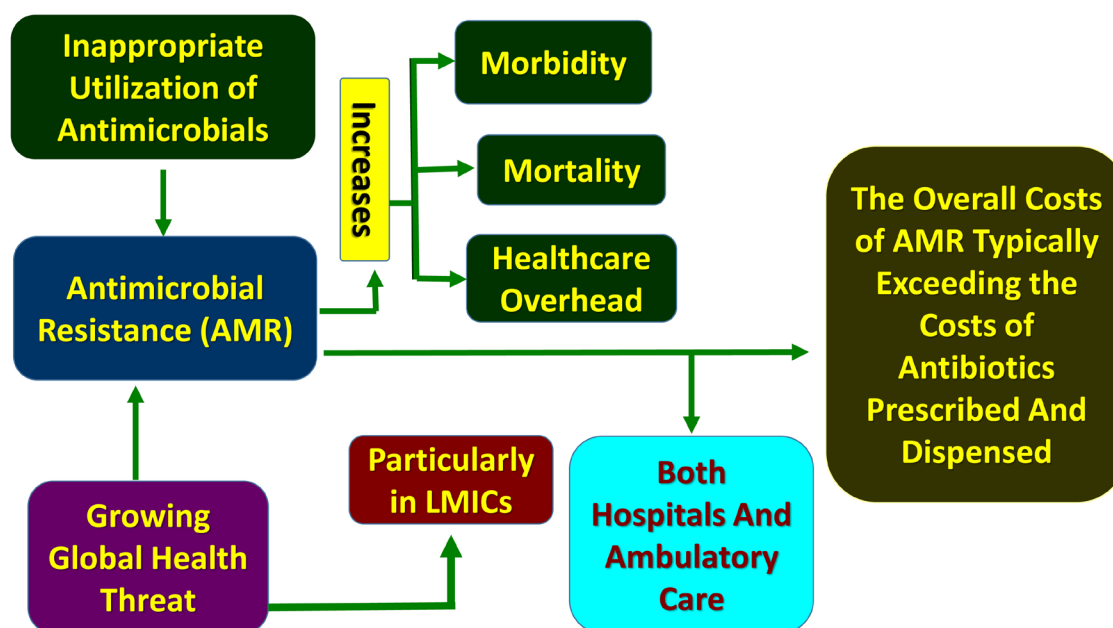
Antimicrobial resistance (AMR) is a growing problem worldwide, leading to increased morbidity, mortality and costs<sup>1-6</sup>, with the overall costs of AMR typically exceeding the costs of the different antibiotics prescribed and dispensed<sup>7</sup>. AMR is particularly important in lower- and middle-income countries (LMICs) as these countries have the highest burden of infectious diseases with growing rates of resistant organisms<sup>8-12</sup>. The concerns with AMR have resulted in multiple initiatives internationally, regionally and nationally, to reduce resistance rates, which include country specific National Action Plans (NAPs)<sup>13-17</sup>. Bangladesh is no exception with its NAP launched in 2017<sup>18</sup>. The Global Antibiotic Resistance Partnership (GARP)-Bangladesh national working group report, published in 2018, also identified a number of activities that should be undertaken in Bangladesh to address concerns with inappropriate utilization of antimicrobials resulting in high resistance rates to commonly prescribed antibiotics and organisms including amoxicillin, cloxacillin, carbapenem, ceftriaxone, and metronidazole as well as *S. pneumoniae*<sup>8,19</sup>. Issues to address include high rates of inappropriate prescribing of antimicrobials in both hospitals and ambulatory care, with self-purchasing

of antibiotics also common in Bangladesh<sup>8,20-24</sup>. Self-purchasing is enhanced among village pharmacies in rural areas of Bangladesh, and wider, as community pharmacists are a trusted source for information. The high co-payments for care in Bangladesh, which can be catastrophic for some families when members become ill<sup>25,26</sup>, can also be reduced by avoiding physician payments. Alongside this, community pharmacies are often more convenient for patients as they are typically open longer hours than primary healthcare clinics. Figure 1 consolidates these different strands to highlight why addressing AMR is a key priority in Bangladesh and across countries, and why both sectors are important going forward.

In this editorial, we will just concentrate on potential programmes to improve antimicrobial use in hospitals. This builds on recent publications on potential ways to tackle AMR in Bangladesh, and more broadly among LMICs, to stimulate future debates<sup>19,27</sup>. This is because we are aware that there can be concerns regarding the extent of antimicrobial stewardship programmes (ASPs) and other activities among hospitals in Bangladesh, acknowledging that ASPs are more difficult to introduce in LMICs due to manpower and cultural issues<sup>8,10,27-32</sup>. In addition,

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**Figure 1:** Key Issues Associated with Rising Antimicrobial Resistance.

there can be multiple prescribing of antibiotics to patients in hospitals in Bangladesh, which can often be inappropriate<sup>8</sup>. Alongside this, hospital physicians in LMICs often gain their knowledge about antimicrobials from pharmaceutical companies, and are influenced by them<sup>33-37</sup>, with physicians in Bangladesh no exception<sup>38,39</sup>. There can also be limited knowledge regarding ASPs among physicians in LMICs versus higher-income countries<sup>40-42</sup>, building on variable knowledge generally regarding antibiotics among healthcare workers and students in LMICs including Bangladesh<sup>43-46</sup>. Consequently, this first editorial of two will just concentrate on potential ways to improve antibiotic prescribing in hospitals.

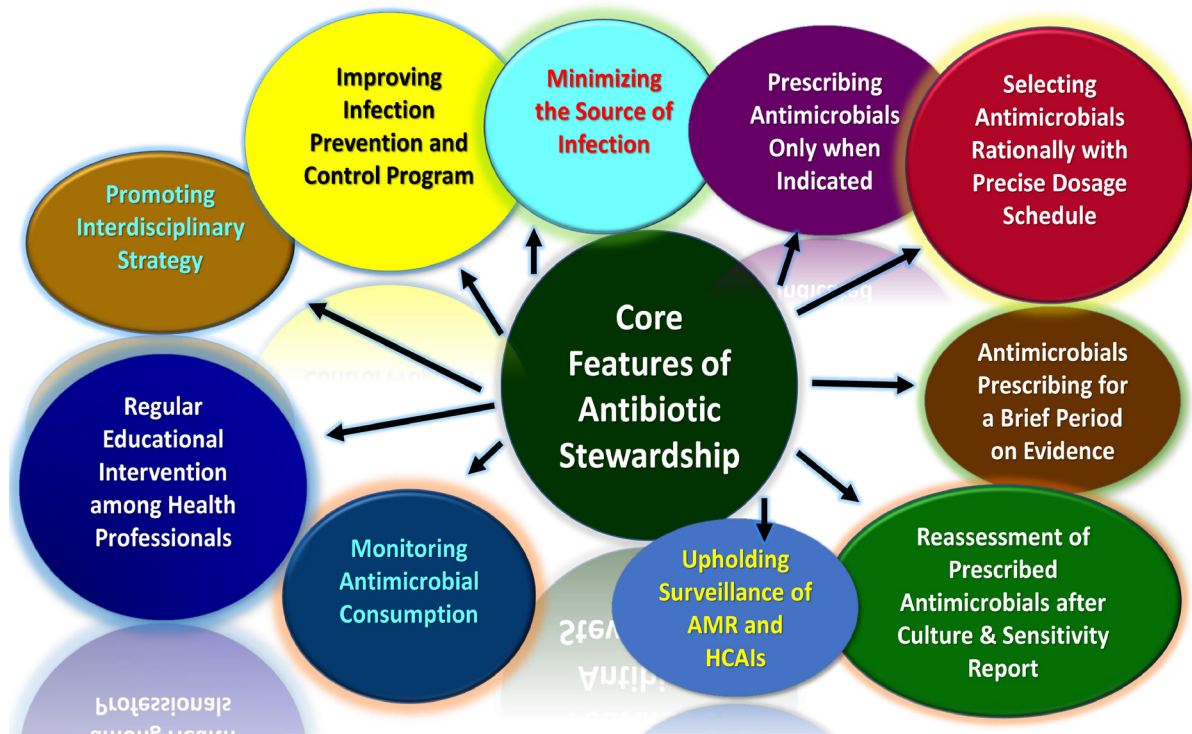
The first step to improve antibiotic utilization in hospitals is to gain a good understanding of current utilization patterns<sup>19</sup>. This includes undertaking point prevalence surveys (PPS) within hospitals, which help document current antimicrobial use among in-patients. The Global PPS studies are the most well-known surveys, which do include hospitals from across Asia<sup>47</sup>. More recently, Saleem *et al.* (2020) undertook a systematic review of PPS studies globally, including Asia, and found that antimicrobial use was appreciably higher in non-European versus European hospitals which is a concern<sup>48</sup>. Undertaking such PPS studies can identify key areas for future quality improvement programmes within hospitals<sup>47,49-51</sup>. Key areas can include addressing the extent of hospital acquired infections (HAIs)

with their implications for increasing length of stay and costs<sup>52-56</sup>. Alongside this, addressing the extent of inadequate physician documentation in patients' notes where this exists including the rationale for any antibiotic prescriptions, the lack of regular reviews of antibiotic usage including IV to oral switches, issues with the timing and length of antibiotic usage to reduce surgical site infections (SSIs) as well as concerns generally with adherence to local, regional or national antibiotic guidelines<sup>49,50,57-59</sup>.

A key area to start with in hospitals to reduce inappropriate use of antibiotics is their prescribing to prevent SSIs<sup>60</sup>. This is because SSIs are currently the most common infectious complications seen among hospitalized patients in LMICs<sup>61,62</sup>, early antibiotic administration has limited effectiveness, and prolonged administration after the operation increases AMR and adverse reactions without reducing SSI rates<sup>63-65</sup>. Despite this, inappropriate use of antibiotics to prevent SSIs is common among LMICs<sup>63</sup>. Several studies have now shown that appropriate educational activities accompanied by policies, guidelines and targets, as well as monitoring subsequent prescribing activities, can appreciably reduce inappropriate antibiotic prescribing and costs associated with SSIs among a range of LMICs<sup>63</sup>. As a result, providing guidance to hospitals in Bangladesh seeking to enhance their prescribing of antimicrobials to prevent SSIs as part of generally reducing HAIs.

Adherence to agreed guidelines is also increasingly seen as an important marker of the quality of antibiotic prescribing within hospitals<sup>47,58,66-68</sup>. However, guidelines must be readily available, updated, easy-to-use and trusted to enhance their use in practice<sup>69-71</sup>. In addition, based on local antibiograms to improve empiric antibiotic prescribing whilst waiting for culture and sensitivity results<sup>56,72</sup>. Other quality indicators can centre around the AWaRe list of antibiotics, documentation and review rates, and early switching to oral antibiotics where pertinent<sup>59,73-77</sup>. However, any quality indicators developed must be easy to implement, measurable and agreed by all key stakeholders to enhance their use and impact<sup>78,79</sup>.

All these initiatives can be part of ASPs within hospitals, and included within the remit of infection, prevention and control groups within hospitals<sup>80,81</sup>. Alternatively, part of the remit of Drug and Therapeutic Committees (DTC)<sup>19</sup>. The introduction of ASPs within hospitals has appreciably reduced inappropriate antibiotic use and costs<sup>10,67,82-85</sup>. In their recent review, Majumder *et al.* (2020) discussed the nine core elements of any ASP, and how they align with the ten essential services of public health, endorsed within the Bangladesh NAP and the GARP-Bangladesh National Working Group<sup>10,18,19</sup> (Figure 2). A critical element of any ASP is a shared responsibility among all key stakeholders within a hospital<sup>10</sup>.



**Figure 2:** Core Elements of Any Antimicrobial Stewardship Program [Adapted from Majumder *et al.*<sup>10</sup>]. HCAs=Health Care Associated Infections

Researchers in LMICs are starting to assess adherence to national strategies in hospital facilities to further reduce AMR rates<sup>86</sup>, and we see this continuing. Clinical pharmacists in hospitals can also play key educational and orchestrational roles driving forward ASPs as part of DTC and other activities<sup>29,87</sup>. They can also co-ordinate therapeutic interchange policies to select potential replacement antibiotics if there are shortages, which are occurring more often with supply and other problems<sup>88,89</sup>. However, this will require more intensive training on clinical pharmacy

and antimicrobials as part of undergraduate courses and post qualification. This has been a concern with pharmacy education in Bangladesh typically industry based with an appreciable proportion of the BPharm curriculum focusing on pharmaceutical science and industry-based courses rather than clinical issues including AMR. However, this is beginning to change, and can build on models for good pharmacy management in the community<sup>90,91</sup>.

In conclusion, it is important that all key stakeholders work together in hospitals in Bangladesh to improve

future antibiotic utilisation and reduce AMR, which is in line with the NAP and GARP-Bangladesh National Working Group<sup>18,19</sup>. This is key to reducing future morbidity, mortality and costs associated with AMR. We have witnessed the catastrophic consequences of COVID 19 arising from misinformation regarding hydroxychloroquine and antibiotics, increasing costs and mortality with no subsequent patient benefit despite the initial hype<sup>22,92-96</sup>. In addition, concerns with treatments such as remdesivir and lopinavir/ritonavir being proposed without a solid evidence-

base, which also showed little benefit in reality in well-constructed clinical trials<sup>92,97,98</sup>. Consequently, it is important that key stakeholders work together in an evidence-based environment to introduce well proven activities to improve future antibiotic utilisation within their hospitals, and continually monitor their outcome to reduce AMR. Alongside this, work together to address misinformation and its consequences. This is the only proven way to reduce AMR rates in hospitals in Bangladesh. We will be looking to monitor such activities in future.

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